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14. ABSTRACT

The Genitourinary Cancer Biorepository at the University of Washington joined the Prostate Cancer Pathology Resource Network (PCBN) September 30th 2014. The purpose of this interaction is to provide high quality, well annotated specimens that can be used by prostate cancer researchers through the PCBN. The University of Washington Biorepository has a focus on advanced stage disease. Specimens provided by the University of Washington site includes blood (serum, plasma, and buffy coat), prostatectomy tissues (frozen), biopsies and metastatic tissue from rapid autopsies (paraffin embedded material and tissue microarrays (TMAs)), prostate cancer patient derived xenografts (PDX) and derived specimens (DNA and RNA) from prostate cancer patients. These specimens are linked to clinical and outcome data and supported by an informatics infrastructure. In this 1st year of operation the University of Washington Site has accrued new specimens from the clinic, surgery, and at autopsy, developed new PDX models, manufactured and provided TMAs, and derived RNA and DNA where required. In addition, we have provided material to conduct biospecimen science research in collaboration with the Johns Hopkins University site and specimens were made available to prostate cancer researchers through the PCBN.

15. SUBJECT TERMS
Biorepository, prostatectomy, Rapid Autopsy, patient derived xenografts

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Introduction

The Prostate Cancer Biorepository Network (PCBN) is a public bioresource that provides high quality, well annotated specimens that can be used by prostate cancer researchers through the PCBN http://prostatebiorepository.org. This biorepository is a collaborative effort between Johns Hopkins University (JHU), New York University (NYU), Memorial Sloan Kettering Cancer Center (MSKCC), University of Washington (UW), Washington University (WU), and the Department of Defense. The PCBN coordinating center is at JHU. UW is a network site.

The Genitourinary Cancer Biorepository at the University of Washington joined the Prostate Cancer Pathology Resource Network (PCBN) September 30th 2014. The UW Prostate Cancer Program has a 25 year history of collecting and distributing biospecimens to investigators worldwide. During that time the University of Washington Biorepository has focused on advanced stage disease. Access to clinical specimens from patients with advanced disease can be challenging so the Genitourinary Cancer Biorepository set up a rapid autopsy program to provide access to metastatic tissue and create patient derived xenograft (PDX) models of advanced disease. The biorepository also has an extensive collection of blood (serum, plasma, and buffy coat), prostatectomy tissues (frozen), and derived specimens (DNA and RNA) from prostate cancer patients; these specimens are linked to clinical and outcome data and supported by an informatics infrastructure.

Keywords

Biorepository, prostate cancer, patient derived xenografts, rapid autopsy, biomarkers.

Accomplishments

The Major goals of the project were (1) patient accrual and biospecimen acquisition, (2) providing specimens to external investigators, and (3) improving biospecimen science.

Patient Accrual and Biospecimen Acquisition: The adjacent table shows specimens prospectively accrued to the PCBN through the University of Washington during the 12 month period covered by this report. African American comprised only 4% of the patient specimens we accrued at UW. This is due to the limited number of African American patients at the UW Medical Center.

Biospecimen Acquisition October 2014 - September 2015	Total Specimens Collected
Serum	
Pre-RRP	104
Metastatic	61
Total	**165**
Tissue	
Prostatectomy	92
Metastatic Sites Sampled	201
Normal Sites Sampled	48
CTC	1
Metastatic Biopsy	24
Total	**369**

Radical prostatectomies: During the year we prepared frozen OCT embedded tissues from 92 prostatectomies. Seventeen were from high risk patients (Gleason 8 and above), 62 were from medium risk (Gleason 7) and 9 were low risk (Gleason 6). Four had an undetermined Gleason due to prior hormone and radiation treatment. Four of the patients were on active surveillance.

Rapid autopsies: We performed eight rapid autopsies during the last year. The prostate cancer patients are approached by oncologists in the clinic and through the altruism and generosity of the patients and their families

as soon as the patient passes we dispatch an ambulance to pick up the body and bring it back to the University of Washington where our autopsy team is prepared for a rapid autopsy and tissue acquisition. Based on our historic data we typically expect 8 autopsies a year and we have performed 8 in the last year. All specimens have been processed and read by a pathologist.

Circulating Tumor Cells (CTC): We only collected one positive specimen during the year. We have determined that we will be unable to isolate a sufficient number of cells to make this resource relevant and therefore will no longer attempt collection unless an effective technology for the identification and isolation of intact CTC becomes available.

Serum and Plasma Isolation: Sera were obtained from 104 prostatectomy patients and 61 metastatic patients. Plasma and buffy coats were obtained from 104 prostatectomy patients and 24 metastatic patients.

Metastatic Biopsies: Working with Dr. Bruce Montgomery we have obtained paraffin embedded metastatic biopsies from 24 patients.

Tissue Microarrays: We have manufactured a PCBN specific metastasis TMA. The TMA consists of 2 bone and 2 visceral metastases (where available) from each of 45 patients. This TMA is of the most recent rapid autopsies available – de-identified clinical data has also been abstracted. Additionally a TMA of 30 LuCaP models has been constructed. The array consists of 3 tumors/ PDX line with 3 cores/ tumor.

Patient Derived Xenografts: We have implanted tissues from primary prostate from 11 African American patients, 3 patients from the operating room and 5 rapid autopsy patients. We have established two lines LuCaP 189.3 (adrenal metastasis) and LuCaP 189.4 (rib metastasis). For additional xenografts it is too early to determine if a line has been established or not.

DNA/RNA Isolation: RNA was isolated from 16 benign prostate tissues, 20 primary prostate cancers, 46 metastases, and 10 normal tissue types.

Providing Specimens to External Investigators:
We have provided serum samples from 108 non-recurrence and 104 recurrent prostate cancer patients (based on rising PSA) were provided to Dr. Neil Bhowmick. Ten Gleason 4+3, 10 Gleason 3+3, 10 normal, and 10 metastatic RNA tumor specimens to Dr. Girish Shukla. Fifty normal and 50 cancer serum specimens to Dr. Robert Veltri. RNA from 15 normal, 15 primary, and 15 metastatic prostate cancer specimens to Dr. Shawn Lupold. LuCaP 86.2 RNA to Dr. Stephanie Green.

Improving Biospecimen Science:
Quality Assurance Study: In discussions with Dr. De Marzo agreement was reached to create 2 LuCaP xenograft series TMAs to assess the effect of sectioning and the storage of tumor specimens on antigenicity. The LuCaP xenograft tissues are a perfect model to test this in. Drs. Corey, Morrissey and De Marzo discussed and designed a template of the first TMAs to assess the stability of protein and RNA over 5 years. The availability of the LuCaP PDX paraffin blocks over prolong period of time is a great resource to perform this stability study. We selected 4 different tumors with variable AR, TMPRSS2/ERG, PTEN and MYC expression and used 3 different tumors and 5-8 cores for each within the 5 year period. The TMA blocks were constructed and sent to Dr. De Marzo for analysis.

Impact

Biospecimens from the clinic, operating room and at autopsy were collected for future use by the prostate cancer research community. New PDX models were developed, and clinical specimens and associated data

were provided to researchers. In addition, we adjusted our approach to the storage of sections from TMA blocks. Based on the work of Dr. De Marzo, now when sectioned from a paraffin block, tissue sections are stored in the -20^{0}C freezer until use.

Changes/Problems

During the year Dr. Vessella retired and was replaced by Dr. Morrissey as the PI on the project. In addition, Dr. Lawrence True replaced Dr. Maria Tretiakova as the lead pathologist on the project. Dr. Xiaotun Zhang went on to a residency and was replaced by Dr. Kristine Von Maltzan. These changes in personnel, the timing of some of the rapid autopsies, providing computing support, and the initial timeframe for obtaining HRPO approval did impact expenditures for year 1.

Products

The reportable outcomes for the project include tissue acquisition, PDX development, and TMA construction, are already discussed under accomplishments.

Participants & other Collaborating Organizations

As stated in accomplishments under 'Improving Biospecimen Science' Dr. Corey has interacted with Dr. DeMarzo to assess protein and RNA stability in tissue blocks over time.

Special Reporting Requirements
N/A

Appendices

The importance of clinically relevant rapid autopsy specimens and LuCaP patient-derived xenograft models to interrogate the heterogeneous and evolving treatment resistance of castration-resistant prostate cancer. Colm Morrissey, Ming H. Lam, Tia S. Higano, Lawrence D. True, Martine Roudier, Robert B. Montgomery, Peter S. Nelson, Paul H. Lange, Evan Y. Yu, Robert L. Vessella, Eva Corey. [Abstract of a poster presentation at the American Association of Cancer Research, Philadelphia PA. April 2015].